REMARKS/ARGUMENTS

Claims 42, 58, 60, and 64 have been amended, claims 79 and 80 have been added, and claims 48-51 and 53 have been cancelled. Support for these amendments and new claims can be found throughout the specification, and in the original and previously presented claims, as described below. Therefore, no new matter has been added by way of claim amendment or presentation of new claims. Entry of these amendments and new claims into the above-identified application is respectfully requested.

Claim 42 has been amended to incorporate the limitation that the targeting molecule comprises the amino acid sequence selected from the group consisting of SEQ ID NOS:114, 115, 116, 117, 118, and 119. Support for this amendment may be found in cancelled claim 48.

Claims 58 and 60 have been amended to remove extra spaces between characters.

Claim 64 has been amended for clarity to change the phrase "an intracellular or extracellular enzyme associated with or secreted from an epithelial barrier," to recite "an intracellular enzyme or an extracellular enzyme associated with or secreted from an epithelial barrier."

New claims 79 and 80 have been added to provide claims directed to the same subject matter as cancelled claims 48-51 and 53. Accordingly, support for these new claims may therefore be found in cancelled claims 48-51 and 53.

Claims 42-47, 52, 54-69, and 73-80 are pending in the application. Reexamination and reconsideration of the claims are respectfully requested in view of the following remarks. The Examiner's comments in the Office Action are addressed below in the order set forth therein.

Maintained Double-Patenting Rejections

Applicants note that the Examiner has maintained rejections of claims 42-48, 52-69, and 73-77 under the judicially-created doctrine of obviousness-type double patenting as being unpatentable over the claims of co-pending U.S. Patent Application No 08/782,481. As stated in the Reply to the Office Action dated December 22, 2003, when the Examiner deems the claims of the present application to be allowable except for this rejection, Applicants will file a

terminal disclaimer in the present case, disclaiming any patent term beyond the term of these patents.

Applicants note that the Examiner has maintained rejections of claims 42-69 and 73-77 under the judicially-created doctrine of obviousness-type double patenting as being unpatentable over the claims of U.S. Patent No. 6,440,419 and co-pending U.S. Patent Application No. 10/062,467. As stated in the Reply to the Office Action dated December 22, 2003, when the Examiner deems the claims of the present application to be allowable except for this rejection, and when the claims of either or both of the co-pending applications are similarly deemed to be allowable, Applicants will file a terminal disclaimer in the present application.

The Rejection of the Claims Under 35 U.S.C. §112 Should Be Withdrawn

Claims 42, 43, 45, 52, 54-65, 67-69, 73, 74, 76, and 77 have been rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that the Examiner contends is not described in the specification in a way as to reasonably convey to one of skill in the art that the inventors, at the time the application was filed, had possession of the claimed invention. The rejection is respectfully traversed for the reasons described below.

The Examiner contends that Applicant's previous argument is unpersuasive relating to the incorporation of structural features necessary for a targeting molecule into the claims. Specifically, in spite of the fact that Applicants amended the claims to recite that the targeting molecule comprises a polypeptide that forms a closed covalent loop and contains at least three peptide domains having beta-sheet character, each of the domains being separated by domains lacking beta-sheet character, the Examiner states that there are no structural or functional limitations to the portion of the J chain. Based upon this argument, the Examiner states that it cannot be ascertained which of the SEQ ID NOS in the dependent claims constitute the minimal structure required to generate an SC-binding site.

Applicants wish to point out that the present invention is based upon the surprising discovery that a J chain or derivative or variants thereof can specifically bind to a factor preferentially distributed on an epithelial surface (e.g., a basolateral factor)(see, e.g., page 8, line

23 to page 9, line 10 of the specification). Applicants not only made this discovery, but also identified a fragment of the J chain that mediates this activity. Specifically, Applicants have identified that domain 2 is responsible for the ability to specifically bind to a factor preferentially distributed on an epithelial surface (e.g., a basolateral factor), and that domain 2 is characterized by a closed covalent loop containing at least three peptide domains having beta-sheet character, each domain separated from the other by a domain lacking beta-sheet character (see, e.g., page 12, lines 8 to 18 of the specification).

Although Applicants disagree with the Examiner, in the interest of expediting prosecution, Applicants have amended claim 42 to recite wherein said targeting molecule comprises the amino acid sequence selected from the group consisting of SEQ ID NOS: 114, 115, 116, 117, 118, and 119. Former claim 49 has been reintroduced as new claim 79 with the added limitation wherein said targeting molecule comprises the amino acid sequence encoded by nucleotides selected from the group consisting of nucleotides 1-414 of SEQ ID NO:7 and nucleotides 1-213 of SEQ ID NO:8. All of the pending claims depend from one of these two claims.

Because all of the pending claims that correspond to claims 42, 43, 45, 52, 54-65, 67-69, 73, 74, 76, and 77 have been amended to recite specific SEQ ID NOS, Applicants respectfully submit that this rejection has been obviated. Accordingly, the rejection of claims 42, 43, 45, 52, 54-65, 67-69, 73, 74, 76, and 77 under 35 U.S.C. § 112, first paragraph should be withdrawn.

Claims 42, 43, 45, 52, 54-65, 67-69, 73, 74, 76, and 77 are also rejected under 35 U.S.C. § 112, first paragraph as containing subject matter that the Examiner contends is not described in the specification in a way as to reasonably enable one of skill in the art to make or use the claimed invention. The rejection is respectfully traversed for the reasons described below.

The Examiner contends that while the specification is enabling for a targeting molecule comprising a J chain and the CH2 and CH3 domains of IgA or IgM, it does not reasonably provide enablement for a targeting molecule comprising a polypeptide that forms a closed covalent loop and contains at least three peptide domains having beta-sheet character, each of the domains being separated by domains lacking beta-sheet character, comprises at least domain 2 of

a J chain, and does not contain any of $C_H1\alpha$, $C_H2\alpha$, $C_H3\alpha$ and C_L. Based upon this argument, the Examiner states that it cannot be ascertained which of the SEQ ID NOS in the dependent claims constitute the minimal structure required to generate an SC-binding site.

As described above, Applicants wish to point out that the present invention is based upon the surprising discovery that a J chain or derivative or variants thereof can specifically bind to a factor preferentially distributed on an epithelial surface (e.g., a basolateral factor)(see, e.g., page 8, line 23 to page 9, line 10 of the specification). Applicants not only made this discovery, but also identified a fragment of the J chain that mediates this activity. Specifically, Applicants have identified that domain 2 is responsible for the ability to specifically bind to a factor preferentially distributed on an epithelial surface (e.g., a basolateral factor), and that domain 2 is characterized by a closed covalent loop containing at least three peptide domains having beta-sheet character, each domain separated from the other by a domain lacking beta-sheet character (see, e.g., page 12, lines 8 to 18 of the specification).

As described above, although Applicants disagree with the Examiner, in the interest of expediting prosecution, Applicants have amended claim 42 to recite wherein said targeting molecule comprises the amino acid sequence selected from the group consisting of SEQ ID NOS: 114, 115, 116, 117, 118, and 119. Former claim 49 has been reintroduced as new claim 79 with the added limitation wherein said targeting molecule comprises the amino acid sequence encoded by nucleotides selected from the group consisting of nucleotides 1-414 of SEQ ID NO:7 and nucleotides 1-213 of SEQ ID NO:8. All of the pending claims depend from one of these two claims.

Because all of the pending claims that correspond to claims 42, 43, 45, 52, 54-65, 67-69, 73, 74, 76, and 77 have been amended to recite specific SEQ ID NOS, Applicants respectfully submit that this rejection has been obviated. Accordingly, the rejection of claims 42, 43, 45, 52, 54-65, 67-69, 73, 74, 76, and 77 under 35 U.S.C. § 112, first paragraph should be withdrawn.

Compliance With Sequence Rules

The Examiner states that the application is not in compliance with the sequence rules because claims 48, 53, 55, 58, and 60 recite SEQ ID NOS:114-140 although SEQ ID NOS:114-

140 are not part of the Sequence Listing. Applicants submit concurrently herewith a Sequence Listing comprising SEQ ID NOS:1-140. This Sequence Listing is identical to the Sequence Listing submitted with the Amendment filed August 19, 2003, with the exception that SEQ ID NO:13 has been corrected, and SEQ ID NOS:114-140 have been added, as described elsewhere herein. Accordingly, the application is now in compliance with the sequence rules.

The Rejection of the Claims Under 35 U.S.C. §§102(b) and 103(a) Should Be Withdrawn

Claims 42, 43, 45, 52, 54, 56, 57, 59, 63, 67-69, 73, 74, 76, and 77 are rejected under 35 U.S.C. §102(b) as being anticipated by Wallner *et al.* (WO 92/16622). The rejection is respectfully traversed for the reasons described below.

As stated by the Examiner, Wallner *et al.* discloses fusion proteins containing a portion of LFA-3 containing a functional CD2-binding domain fused to at least a portion of the Fc region of an immunoglobulin. The Fc region is preferably limited to the hinge region of the CH2 and CH3 domains. In addition, Wallner *et al.* discloses multimeric forms of LFA-3-Ig fusion proteins generated by using those Fc regions, or portions thereof, of Ig molecules that are usually multivalent, e.g., IgM pentamers and IgA dimers. Wallner *et al.* states that a J chain polypeptide may be necessary to form and stabilize IgM pentamers and IgA dimers.

Applicants have amended claim 42 to recite wherein said targeting molecule comprises the amino acid sequence selected from the group consisting of SEQ ID NOS: 114, 115, 116, 117, 118, and 119. Former claim 49 has been reintroduced as new claim 79 with the added limitation wherein said targeting molecule comprises the amino acid sequence encoded by nucleotides selected from the group consisting of nucleotides 1-414 of SEQ ID NO:7 and nucleotides 1-213 of SEQ ID NO:8. All of the pending claims depend from one of these two claims.

Wallner *et al.* does not teach use of a targeting molecule that comprises the amino acid sequence selected from the group consisting of SEQ ID NOS: 114, 115, 116, 117, 118, and 119, or the amino acid sequence encoded by nucleotides selected from the group consisting of nucleotides 1-414 of SEQ ID NO:7 and nucleotides 1-213 of SEQ ID NO:8. Wallner *et al.* therefore does not meet all of the limitations of the pending claims in the present application. To

anticipate a claim, a reference must teach every element of the claim. *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Accordingly, Applicants respectfully request that the rejection of claims 42, 43, 45, 52, 54, 56, 57, 59, 63, 67-69, 73, 74, 76, and 77 under 35 U.S.C. §102(b) be withdrawn.

In the alternative, claims 42, 43, 45, 52, 54, 56, 57, 59, 63, 67-69, 73, 74, 76, and 77 are rejected under 35 U.S.C. §103(a) as being obvious in view of Wallner *et al.* The rejection is respectfully traversed for the reasons described below.

The Examiner states that if Wallner *et al.* were construed as disclosing multimeric forms of LFA-3-Ig fusion proteins generated by using those Fc regions, or portions thereof, of Ig molecules that are normally multivalent, e.g., IgM pentamers and IgA dimers that do not comprise a J chain, that it would have been obvious to one of ordinary skill in the art to modify Wallner *et al.* by incorporating a J chain with a reasonable expectation of success. However, Applicants have amended claim 42 and reintroduced former claim 49 as new claim 79, as described above. All of the pending claims depend from one of these two claims.

To establish a *prima facie* case of obviousness: 1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or combine the reference teachings; 2) there must be a reasonable expectation of success; and 3) the prior art reference(s) must teach or suggest all the claim limitations. MPEP §2143, citing *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991). The Examiner bears the initial burden of factually supporting any *prima facie* conclusion of obviousness, and if the examiner does not produce a *prima facie* case, the applicant is under no obligation to submit evidence of nonobviousness. MPEP §2143, citing *Ex parte Clapp*, 227 USPQ 972, 973 (Bd. Pat. App. & Inter. 1985). It is Applicants' contention that a *prima facie* case of obviousness has not been established for the rejection set forth above.

Wallner *et al.* does not teach or suggest that SEQ ID NOS: 114, 115, 116, 117, 118, and 119, or the amino acid sequences encoded by nucleotides selected from the group consisting of nucleotides 1-414 of SEQ ID NO:7 and nucleotides 1-213 of SEQ ID NO:8, are particularly important for binding to or facilitating binding to an epithelial basolateral factor. Furthermore,

the Examiner has not presented any evidence that one of skill in the art, reading Wallner *et al.*, would be motivated to focus on SEQ ID NOS: 114, 115, 116, 117, 118, and 119, or the amino acid sequence encoded by nucleotides selected from the group consisting of nucleotides 1-414 of SEQ ID NO:7 and nucleotides 1-213 of SEQ ID NO:8. Therefore, amended claim 42, new claim 79, and their dependent claims are not rendered obvious in view of Wallner *et al.*

Because Wallner *et al.* does not teach or suggest all the claim limitations of any of the pending claims in the present application, a *prima facie* case of obviousness has not been established. Accordingly, the rejection of claims 42, 43, 45, 52, 54, 56, 57, 59, 63, 67-69, 73, 74, 76, and 77 under 35 U.S.C. §103(a) should be withdrawn.

In view of the above arguments, all grounds for rejection under 35 U.S.C. §§ 102(b) and 103(a) have been overcome. Reconsideration and withdrawal of the rejections are therefore respectfully requested.

The Rejection of the Claims Under 35 U.S.C. §102(e) Should Be Withdrawn

Claims 73, 74, 76, and 77 have been rejected under 35 U.S.C. §102(e) as being anticipated by Capra (U.S. Patent No. 6,063,905). The rejection is respectfully traversed for the reasons described below.

The Examiner describes Capra as disclosing an IgA antibody consisting essentially of a VH domain fused to a first IgA1 Cα3 domain including a tailpiece, a VL domain fused to a second IgA1 Cα3 domain including a tailpiece, and a J chain, wherein the VL and VH domains constitute an antigen or hapten recognition site. The invention may further be defined as the dimers of the described minimal IgA antibodies formed by disulfide bonds between the monomers and the J chains and across the tailpieces. Therefore, the Examiner states that Capra discloses a molecule comprising a J chain covalently linked via a peptide bond to an antigen combining site that does not contain any of $C_H1\alpha$, $C_H2\alpha$, $C_H3\alpha$ and C_L.

Applicants have amended claim 42 as described above. Claims 73, 74, 76, and 77 depend from currently amended claim 42. Capra does not teach use of a targeting molecule that comprises the amino acid sequence selected from the group consisting of SEQ ID NOS: 114,

115, 116, 117, 118, and 119, or the amino acid sequence encoded by nucleotides selected from the group consisting of nucleotides 1-414 of SEQ ID NO:7 and nucleotides 1-213 of SEQ ID NO:8. Capra therefore does not meet all of the limitations of the pending claims in the present application. To anticipate a claim, a reference must teach every element of the claim. *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Accordingly, Applicants respectfully request that the rejection of claims 73, 74, 76, and 77 under 35 U.S.C. §102(b) be withdrawn.

The Rejection of the Claims Under 35 U.S.C. §103(a) Should Be Withdrawn

Claims 42 and 54-60 have been rejected under 35 U.S.C. §103(a) as being obvious in view of Wallner *et al.* in combination with Chamow & Ashkenazi (1996) *Trends in Biotechnology*, 14:52-60 and Max & Korsmeyer (1985) *J. Exp. Med.* 161:832-849. The rejection is respectfully traversed for the reasons described below.

The Examiner describes Wallner *et al.* as teaching multimeric forms of LFA-3-Ig fusion proteins generated by using Fc regions, or portions thereof, of Ig molecules that are usually multivalent, e.g., IgM pentamers and IgA dimers, that may comprise a J chain, and methods of making these fusion proteins through recombinant means, but not a human J chain. The Examiner states that Max & Korsmeyer teaches an isolated nucleic acid molecule encoding the amino acid sequence of SEQ ID NOS:125, 130, 131, 133, 135, and AsnLys. Furthermore, the Examiner states that Chamow & Ashkenazi teach that human antibodies are less immunogenic than mAbs derived from non-human species and that immunoadhesins circumvent the difficulty in obtaining human antibodies.

Applicants have amended claim 42 to recite wherein said targeting molecule comprises the amino acid sequence selected from the group consisting of SEQ ID NOS: 114, 115, 116, 117, 118, and 119. Claims 54-60 depend from claim 42.

As stated above, one of the necessary elements for establishing a *prima facie* case of obviousness is that the prior art reference(s) must teach or suggest all the claim limitations. MPEP §2143, citing *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991). The Examiner bears the initial burden of factually supporting any *prima facie* conclusion of obviousness, and if the examiner

does not produce a *prima facie* case, the applicant is under no obligation to submit evidence of nonobviousness. MPEP §2143, citing *Ex parte Clapp*, 227 USPQ 972, 973 (Bd. Pat. App. & Inter. 1985). It is Applicants' contention that a *prima facie* case of obviousness has not been established for the rejection set forth above.

Wallner *et al.*, Max & Korsmeyer, and Chamow & Ashkenazi, individually or in combination, do not teach or suggest that SEQ ID NOS: 114, 115, 116, 117, 118, and 119, or the amino acid sequences encoded by nucleotides selected from the group consisting of nucleotides 1-414 of SEQ ID NO:7 and nucleotides 1-213 of SEQ ID NO:8, are particularly important for binding to or facilitating binding to an epithelial basolateral factor. Furthermore, the Examiner has not presented any evidence that one of skill in the art, reading the combined references, would be motivated to focus on SEQ ID NOS: 114, 115, 116, 117, 118, and 119, or the amino acid sequence encoded by nucleotides selected from the group consisting of nucleotides 1-414 of SEQ ID NO:7 and nucleotides 1-213 of SEQ ID NO:8. Therefore, amended claim 42 and dependent claims 54-60 are not rendered obvious in view of the combination of Wallner *et al.*, Max & Korsmeyer, and Chamow & Ashkenazi.

Because the combination of Wallner *et al.*, Max & Korsmeyer, and Chamow & Ashkenazi does not teach or suggest all the claim limitations of any of the pending claims in the present application, a *prima facie* case of obviousness has not been established. Accordingly, the rejection of claims 42 and 54-60 under 35 U.S.C. §103(a) should be withdrawn.

Claims 42 and 62 have been rejected under 35 U.S.C. §103(a) as being obvious in view of Wallner *et al.* in combination with Chamow & Ashkenazi and Max & Korsmeyer, and in further combination with Cheng (U.S. Patent No. 5,814,507). The rejection is respectfully traversed for the reasons described below.

The Examiner states that Cheng teaches a receptor protein tyrosine phosphatase peptide (PTP)λ, wherein said polypeptide is capable of dephosphorylating phosphorylated tyrosine residues and derivatives of these PTP polypeptides that substantially retain the ability to dephosphorylate phosphorylated tyrosine residues. Covalent derivatives/modifications specifically include fusion proteins comprising native (PTP)λ sequences and their amino acid

sequence variants, such as immunoadhesins. Cheng does not teach multimeric forms of (PTP)λ generated using Fc regions or portions thereof, of Ig molecules that are usually multivalent, e.g., IgM pentamers and IgA dimers, that comprise a human J chain. However, the Examiner states that it would have been obvious to one of skill in the art to modify the teachings of Wallner *et al.*, Chamow & Ashkenazi, and Max & Korsmeyer by substituting (PTP)λ polypeptides.

Applicants have amended claim 42 as described above. Claim 62 depends from currently amended claim 42.

As stated above, one of the necessary elements for establishing a *prima facie* case of obviousness is that the prior art reference(s) must teach or suggest all the claim limitations. MPEP §2143, citing *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991). The Examiner bears the initial burden of factually supporting any *prima facie* conclusion of obviousness, and if the examiner does not produce a *prima facie* case, the applicant is under no obligation to submit evidence of nonobviousness. MPEP §2143, citing *Ex parte Clapp*, 227 USPQ 972, 973 (Bd. Pat. App. & Inter. 1985). It is Applicants' contention that a *prima facie* case of obviousness has not been established for the rejection set forth above.

Wallner *et al.*, Max & Korsmeyer, Chamow & Ashkenazi, and Cheng, individually or in combination, do not teach or suggest that SEQ ID NOS: 114, 115, 116, 117, 118, and 119, or the amino acid sequences encoded by nucleotides selected from the group consisting of nucleotides 1-414 of SEQ ID NO:7 and nucleotides 1-213 of SEQ ID NO:8, are particularly important for binding to or facilitating binding to an epithelial basolateral factor. Furthermore, the Examiner has not presented any evidence that one of skill in the art, reading the combined references, would be motivated to focus on SEQ ID NOS: 114, 115, 116, 117, 118, and 119, or the amino acid sequence encoded by nucleotides selected from the group consisting of nucleotides 1-414 of SEQ ID NO:7 and nucleotides 1-213 of SEQ ID NO:8. Therefore, amended claim 42 and dependent claim 62 are not rendered obvious in light of the combination of Wallner *et al.*, Max & Korsmeyer, Chamow & Ashkenazi, and Cheng.

Because the combination of Wallner *et al.*, Max & Korsmeyer, Chamow & Ashkenazi, and Cheng does not teach or suggest all the claim limitations of any of the pending claims in the

present application, a *prima facie* case of obviousness has not been established. Accordingly, the rejection of claims 42 and 62 under 35 U.S.C. §103(a) should be withdrawn.

Claims 73, 74, 76, and 77 have been rejected under 35 U.S.C. §103(a) as being obvious in view of Max & Korsmeyer in combination with Janknecht & Nordheim (1992) *Gene*, 121:321-324. The rejection is respectfully traversed for the reasons described below.

Examiner states that Max & Korsmeyer teaches an isolated nucleic acid molecule encoding the amino acid sequence of SEQ ID NOS:125, 130, 131, 133, 135, and AsnLys. The Examiner further states that Janknecht & Nordheim teaches the production of eukaryotic proteins in a functional state, using eukaryotic expression systems employing vectors designed to express either N- or C-terminally histidine tagged proteins in eukaryotic cells. Based upon these references, the Examiner states that it would have been obvious to one of skill in the art to recombinantly express the human J chain nucleic acid molecule as taught by Max & Korsmeyer with a His tag as taught by Janknecht & Nordheim.

Applicants have amended claim 42 as described above. Claims 73, 74, 76, and 77 depend from currently amended claim 42.

As stated above, one of the necessary elements for establishing a *prima facie* case of obviousness is that the prior art reference(s) must teach or suggest all the claim limitations. MPEP §2143, citing *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991). The Examiner bears the initial burden of factually supporting any *prima facie* conclusion of obviousness, and if the examiner does not produce a *prima facie* case, the applicant is under no obligation to submit evidence of nonobviousness. MPEP §2143, citing *Ex parte Clapp*, 227 USPQ 972, 973 (Bd. Pat. App. & Inter. 1985). It is Applicants' contention that a *prima facie* case of obviousness has not been established for the rejection set forth above.

Max & Korsmeyer and Janknecht & Nordheim, individually or in combination, do not teach or suggest that SEQ ID NOS: 114, 115, 116, 117, 118, and 119, or the amino acid sequences encoded by nucleotides selected from the group consisting of nucleotides 1-414 of SEQ ID NO:7 and nucleotides 1-213 of SEQ ID NO:8, are particularly important for binding to or facilitating binding to an epithelial basolateral factor. Furthermore, the Examiner has not

presented any evidence that one of skill in the art, reading the combined references, would be motivated to focus on SEQ ID NOS: 114, 115, 116, 117, 118, and 119, or the amino acid sequence encoded by nucleotides selected from the group consisting of nucleotides 1-414 of SEQ ID NO:7 and nucleotides 1-213 of SEQ ID NO:8. Therefore, claims 73, 74, 76, and 77 incorporating the limitations of amended claim 42 are not rendered obvious in light of the combination of Max & Korsmeyer and Janknecht & Nordheim.

Because the combination of Max & Korsmeyer and Janknecht & Nordheim does not teach or suggest all the claim limitations of any of the pending claims in the present application, a *prima facie* case of obviousness has not been established. Accordingly, the rejection of claims 73, 74, 76, and 77 under 35 U.S.C. §103(a) should be withdrawn.

In view of the above arguments, all grounds for rejection under 35 U.S.C. § 103(a) have been overcome. Reconsideration and withdrawal of the rejections are therefore respectfully requested.

The Rejection of the Claims Under 35 U.S.C. §112 Should Be Withdrawn

Claim 51 has been rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that the Examiner contends is not described in the specification in a way as to reasonably convey to one of skill in the art that the inventors, at the time the application was filed, had possession of the claimed invention. The rejection is respectfully traversed for the reasons described below.

The Examiner states that the nucleotide sequence of SEQ ID NO:13 and the associated amino acid sequence differ from the originally filed SEQ ID NO:13 and associated amino acid sequence. Applicants have cancelled claim 51. Therefore, this rejection has been rendered moot.

Claims 64 and 65 have been rejected under 35 U.S.C. § 112, second paragraph, on the grounds that they are indefinite for reciting the term "intracellular ... enzyme ... secreted from an epithelial barrier." Applicants have amended claim 64 for clarity to change the phrase "an

intracellular or extracellular enzyme associated with or secreted from an epithelial barrier," to recite "an intracellular enzyme or an extracellular enzyme associated with or secreted from an epithelial barrier." Claim 65 depends from claim 64. Accordingly, the rejection of claims 64 and 65 under 35 U.S.C. § 112, second paragraph has been obviated and should be withdrawn.

The Objection to the Specification Should Be Withdrawn

The Examiner has objected to the amendment filed August 19, 2003 as introducing new matter into the disclosure. Specifically, the nucleotide sequence of SEQ ID NO:13 and the associated amino acid sequence differ from the originally filed SEQ ID NO:13 and associated amino acid sequence. Applicants submit concurrently herewith a Sequence Listing comprising SEQ ID NOS:1-140. This Sequence Listing is identical to the Sequence Listing submitted with the Amendment filed August 19, 2003, with the exception that SEQ ID NO:13 has been corrected, and SEQ ID NOS:114-140 have been added, as described elsewhere herein. Accordingly, the objection to the specification should be withdrawn.

The Objection to Claim 50

Claim 50 has been objected to for depending from a rejected base claim. Claim 50 has been cancelled. Accordingly, this objection has been rendered moot.

CONCLUSION

In view of the aforementioned amendments and remarks, Applicants respectfully submit that the objections to the claims and specification have been obviated, and the rejections of the claims under 35 U.S.C. §§ 112, first and second paragraphs, 102(b), 102(e), and 103(a) are overcome. Accordingly, Applicants submit that this application is now in condition for allowance. Early notice to this effect is solicited.

If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,

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CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on July 22, 2005

Lynda J. Pixley